

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

1. **(Original)** A formulation for targeting an epitope on an antigen expressed in a mammal, the formulation comprising a pharmaceutically acceptable carrier in combination with, a dimeric biosynthetic construct for binding at least one preselected antigen, the construct comprising:

- (a) two polypeptide chains, each of which have: an amino acid sequence defining at least two polypeptide domains, connected by a polypeptide linker spanning the distance between the C-terminus of one domain and the N-terminus of the other, the amino acid sequence of each said domain comprising complementarity determining regions (CDRs) interposed between framework regions (FRs), the CDRs and FRs of each polypeptide chain together defining a binding site immunologically reactive with a said preselected antigen, and
and a C-terminal tail having a non-self-associating structure under physiological conditions and comprising at least a crosslinking means, and
- (b) a linkage coupling said crosslinking means on said two polypeptide chains,

said dimeric construct having a conformation permitting binding of a said preselected antigen by the binding site of each said polypeptide chain when administered to said mammal.

2. **(Original)** A formulation for targeting an epitope on an antigen expressed in a mammal, the formulation comprising a pharmaceutically acceptable carrier in combination with, a dimeric biosynthetic construct for binding preferentially to a preselected antigen, the construct comprising:

- (a) two polypeptide chains, each of which have: an amino acid sequence defining at least two polypeptide domains, connected by a polypeptide linker spanning the distance between the C-terminus of one domain and the N-terminus of the other, the amino acid sequence of each said domain

comprising complementarity determining regions (CDRs) interposed between framework regions (FRs), the CDRs and FRs of each polypeptide chain together defining a binding site immunologically reactive with a said preselected antigen, and

a C-terminal tail having a non-self-associating structure under physiological conditions and comprising at least a crosslinking means, and

- (b) a linkage coupling said crosslinking means to form a homodimeric construct,

said homodimeric construct having a conformation permitting binding to said preselected antigen in said mammal with an avidity greater than the avidity of either of said polypeptide chains individually.

3. **(Original)** A polypeptide chain for binding preferentially to a preselected antigen, the polypeptide chain comprising:

an amino acid sequence defining at least two polypeptide domains, connected by a polypeptide linker spanning the distance between the C-terminus of one domain and the N-terminus of the other, the amino acid sequence of each said domain comprising complementarity determining regions (CDRS) interposed between framework regions (FRs), the CDRs and FRs of each polypeptide chain together defining a binding site immunologically reactive with said preselected antigen, and
a C-terminal tail having a non-self-associating structure under physiological conditions and comprising at least a crosslinking means.

4. **(Original)** The polypeptide chain of claim 1, 2 or 3 wherein said C-terminal tail comprises the amino acid sequence Ser-Cys.

5. **(Currently amended)** The polypeptide chain of claim 1, 2 or 3 wherein said C-terminal tail comprises the amino acid sequence (Gly)₄-Cys represented in SEQ ID NO: 10.

6. **(Currently amended)** The polypeptide chain of claim 1, 2 or 3 wherein said C-terminal tail comprises the amino acid sequence (His)₆-(Gly)₄-Cys represented in SEQ ID NO: 11.

7. **(Original)** The polypeptide chain of claim 1, 2 or 3 wherein said C-terminal tail can chelate one or more ions.
8. **(Original)** The polypeptide chain of claim 7 wherein said ion is a metal ion.
9. **(Original)** The polypeptide chain of claim 1, 2 or 3 wherein said crosslinking means is a derivatizable amino acid side chain.
10. **(Original)** The polypeptide chain of claim 9 wherein said derivatizable amino acid is selected from the group consisting of lysine, arginine and histidine.
11. **(Original)** The polypeptide chain of claim 9 wherein said derivatizable amino acid is a cysteine amino acid.
12. **(Original)** The polypeptide chain of claim 1, 2 or 3 wherein said crosslinking means comprises a posttranslationally modified amino acid.
13. **(Original)** The polypeptide chain of claim 12 wherein said posttranslationally modified amino acid is the Asn residue located in the amino acid sequence selected from group of Asn-Xaa-Ser and Asn-Xaa-Thr.
14. **(Original)** The formulation of claim 1 or 2 wherein said linkage is a chemical bridge.
15. **(Original)** The formulation of claim 1 or 2 wherein said linkage comprises a disulfide bond.
16. **(Original)** The formulation of claim 1 or 2 wherein said linkage comprises a bismaleimido-hexane cross-linker.
17. **(Original)** The formulation of claim 1 or 2 wherein said linkage comprises a

bismaleimidocaproyl amino acid linker.

18. **(Original)** The formulation of claim 1 or 2 wherein said linkage comprises a peptidyl linker.
19. **(Original)** The formulation of claim 1 or 2 wherein said linkage forms a substantially inflexible structure under physiological conditions.
20. **(Original)** The formulation of claim 1 or 2 wherein said linkage has a length and composition optimized for binding of two preselected antigens expressed on a tissue surface in a mammal.
21. **(Original)** The formulation of claim 1 or 2 wherein said linkage comprises a detectable moiety.
22. **(Original)** The formulation of claim 21 wherein said detectable moiety comprises Technetium^{99m}.
23. **(Original)** The formulation of claim 21 wherein said detectable moiety comprises means for inducing proton relaxation in vivo.
24. **(Original)** The formulation of claim 1 or 2 wherein said dimeric biosynthetic construct targets said epitope on said antigen with an avidity greater than that of a monoclonal antibody having the same antigenic determinant as said construct, or a fragment thereof.
25. **(Original)** The formulation of claim 1 or 2 wherein said dimeric biosynthetic construct targets said epitope on said antigen with an avidity greater than that of either of said polypeptide chains individually.
26. **(Original)** The formulation of claim 1 or 2 wherein said preselected antigen is expressed on the surface of a cell.

27. **(Original)** The formulation of claim 1 or 2 wherein said antigen is an intracellular component exposed upon cell lysis.
28. **(Original)** The formulation of claim 1 or 2 wherein said dimeric construct binds two different epitopes.
29. **(Original)** The formulation of claim 1 or 2 wherein one of said binding sites further comprises a catalytic site.
30. **(Original)** The formulation of claim 1 or 2 wherein one of said binding sites binds an epitope on a therapeutic agent to be targeted to a cell surface.
31. **(Original)** The formulation of claim 30 wherein said therapeutic agent is a cytotoxic agent.
32. **(Original)** The formulation of claim 1, 2 or 3 wherein said construct has improved in vivo imaging characteristics.
- 33-49. **(Canceled)**
50. **(New)** A formulation for targeting an epitope on an antigen expressed in a mammal, the formulation comprising a pharmaceutically acceptable carrier in combination with,
a dimeric biosynthetic construct for binding at least one epitope on a therapeutic agent to be targeted to a cell surface, the construct comprising:
- (a) two polypeptide chains, each of which have: an amino acid sequence defining at least two polypeptide domains, connected by a polypeptide linker spanning the distance between the C-terminus of one domain and the N-terminus of the other, the amino acid sequence of each said domain comprising complementarity determining regions (CDRs) interposed between framework regions (FRs), the CDRs and FRs of each polypeptide

chain together defining a binding site immunologically reactive with said at least one epitope on a therapeutic agent to be targeted to a cell surface, and

a C-terminal tail having a non-self-associating structure under physiological conditions and comprising at least a crosslinking means, and

- (b) a peptidyl linker coupling said crosslinking means on said two polypeptide chains,

said dimeric construct having a conformation permitting binding of said at least one epitope on a therapeutic agent by the binding site of each said polypeptide chain when administered to said mammal.